producing cells *in vitro* comprising introducing into the cell a dominant negative allele of a *PMS2*, wherein the dominant negative allele encodes a truncated PMS2 that consists of the first 133 amino acids of PMS2; and (2) a homogeneous culture of isolated, hypermutable antibody-producing cells as described for the method claims. The Office Action alleges that the claims are not commensurate with the scope of the disclosure, such that undue experimentation would be necessary to make and use the invention. Applicants respectfully traverse.

Much of the discussion in the Office Action regarding enablement is drawn to the issue of claims reading on *in vivo* application of the methods and transgenic animals. Without conceding the correctness of the rejection as it may apply to *in vivo* applications of the method or transgenic animals in any continuation or divisional applications, Applicants have amended the method claims in the instant application to include the feature that he method is performed *in vitro*, as helpfully suggested by the Examiner. The Applicants have also amended the claims to the cells in the instant application, as helpfully suggested by the Examiner, to include the feature that the cells are isolated. According to the Office Action (Paper No. 20, page 13) these amendments to the method claims and the cell claims obviates the enablement rejection with respect to reading on *in vivo* methods and transgenic animals, respectfully. Therefore, Applicants request withdrawal of the rejection under 35 U.S.C. §112, first paragraph, on these grounds.

With respect to the other forms of truncation mutants than strictly those consisting of the first 133 amino acids of PMS2, the Applicants believe the Examiner's position is unduly narrow with respect to what is enabled by the Specification for the following reasons, and respectfully urge the Examiner to reconsider.

Amendment filed 7/28/03 OIC to entry 9/11/03

22. (Previously Amended) The method of claim 1 wherein an immunoglobulin gene is co-introduced into said cell, whereby said cell produces said antibodies.

23. (Currently Amended) A homogeneous culture of isolated, hypermutable, mammalian cells wherein said cells [[produces]] produce antibodies and comprise a dominant negative allele of a [[PMS2]] mismatch repair gene, wherein said dominant negative allele encodes a truncation mutant of a PMS2 protein.

24. (Canceled)

25. (Currently Amended) The culture of isolated, hypermutable, mammalian cells of claim 23 wherein the mismatch repair gene is human *PMS2*.

26-28. (Canceled)

29. (Currently Amended) The culture of isolated, hypermutable, mammalian cells of claim 23 wherein the cells express a protein consisting of the first 133 amino acids of hPMS2.

30-72. (Canceled)

73. (Previously added) A cell produced by the method of claim 1.

74. (Previously added) A cell produced by the method of claim 4.

75. (Previously added) The method of claim 1 further comprising the step restoring genetic stability of said hypermutable cell.

76. (Previously added) A cell produced by the method of claim 75.

77. (Previously added) A homogeneous culture of the cells of claim 76.

78. (Previously added) The method of claim 22 further comprising the step restoring genetic stability of said hypermutable cell.

79. (Previously added) A cell produced by the method of claim 78.

80. (Previously added) A homogeneous culture of the cells of claim 79.